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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/518,470	11/14/2005	Moshe Szyf	FC 14647-80	5007
1059 7590 06/13/2007 BERESKIN AND PARR 40 KING STREET WEST BOX 401 TORONTO, ON M5H 3Y2 CANADA			EXAMINER SHIN, DANA H	
			ART UNIT 1635	PAPER NUMBER
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/518,470	<b>Applicant(s)</b> SZYF ET AL.	
	<b>Examiner</b> Dana Shin	<b>Art Unit</b> 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 30 May 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-11 and 20-31 is/are pending in the application.
- 4a) Of the above claim(s) 21 and 22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-11 and 23-31 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Election/Restrictions***

Applicant's election with traverse of claims 1-11 and 22-31 pertaining to SEQ ID NO:10 in the reply filed on May 30, 2007 is acknowledged. The traversal is on the ground(s) that the claims of groups I-IX have a single inventive concept, namely, oligonucleotide inhibitor of a given sequence and a method of using the inhibitor. This is not found persuasive because the "given sequence" claimed in each inventive group is chemically distinct, and furthermore, the inventions listed as groups I-IX were found to lack the same or corresponding special technical features that define a contribution over the prior art of Slack et al. under PCT Rule 13.1.

The requirement is still deemed proper and is therefore made FINAL.

### ***Status of Claims***

Claims 1-11 and 20-31 are pending. Claims 20-21 and SEQ ID NOs:5, 6, 7, 8, 9, 11, 12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Accordingly, claims 1-11 and 22-31 pertaining to SEQ ID NO:10 are currently under examination on the merits.

### ***Claim Objections***

Claims 5, 23, and 26 are objected to for containing non-elected subject matter: SEQ ID NOs:5, 6, 7, 8, 9, 11, and 12. Appropriate correction is required.

***Claim Rejections - 35 USC § 112, first paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5-11, and 22-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and /or chemical properties, functional characteristics, structure/function correlation, or any combination thereof.

In the instant case, the claims recite an oligonucleotide inhibitor. As broadly written, the term “oligonucleotide inhibitor” embraces different classes of nucleic acid-based inhibitors such as antisense oligonucleotides, siRNAs, miRNAs, ribozymes, DNazymes, aptamers, triplexes, and yet-to-be identified oligonucleotide inhibitors. Furthermore, claims 22-31 are directed to *in vivo* methods comprising any oligonucleotide inhibitor targeted to MBD2 gene.

Note that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species. A “representative number of species” means that the species which are adequately described are representative of the entire

genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure “indicates that the patentee has invented species sufficient to constitute the gen[us].” See *Enzo Biochem*, 323 F.3d at 966, 63 USPQ2d at 1615; *Noelle v. Lederman*, 355 F.3d 1343, 1350, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (“[A] patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated.”). See also MPEP §2163.

In light of the above, the instant specification does not clearly allow persons of ordinary skill in the art to recognize that the inventors invented the genus claimed in the instant case, because the specification only discloses antisense oligonucleotide species that inhibit MBD2 expression *in vitro* and *in vivo*. See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1562, 19 USPQ2d 1111, 1115 (Fed. Cir. 1991), which clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” (see page 1117).

Since the specification has failed to describe a representative number of species embraced by the term “oligonucleotide inhibitor”, and since the disclosure demonstrates *in vivo* inhibition of MBD2 expression via antisense oligonucleotides only, it is concluded that the specification does not reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed genus.

Claims 22-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating cancer in a mammal comprising administering an antisense oligonucleotide of SEQ ID NO:12, does not reasonably provide enablement for preventing cancer in a mammal or treating cancer in a mammal by other than oligonucleotide inhibitor comprising SEQ ID NO:12. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). The Court in *Wands* states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'." (*Wands*, 8 USPQ2d 1404). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The claims are drawn to methods of treating or preventing cancer in a mammal *in vivo* comprising administering an oligonucleotide of inhibitor targeted to MBD2/demethylase gene.

The specification provides *in vivo* examples wherein chemically modified antisense oligonucleotide comprising SEQ ID NO:12 (referred to as A10 in the specification, see Table 1 or page 42) reduces tumor volume and growth of lung carcinoma and colorectal carcinoma cells in mice. See Example 5 and 6. In particular, applicant discloses that 7 out of 8 mice were tumor-free after series of treatment with antisense oligonucleotide of SEQ ID NO:12. See page 48. Nevertheless, the effect of the antisense oligonucleotide of SEQ ID NO:12 in “preventing cancer” is not adequately described in the specification because the plain English meaning of the term “prevent” encompasses “stop from occurring”. See Dictionary citation. Furthermore, there is no *in vivo* example wherein applicant’s elected oligonucleotide sequence, SEQ ID NO:10, is capable of treating cancer in a mammal *in vivo*.

The unpredictability of nucleic-acid based drugs (e.g., antisense oligonucleotide, ribozyme, and siRNA) was dominant in the art as of the earliest filing date sought dated June 20, 2002. See for example Opalinska et al. (*Nature Reviews*, 2002, 1:503-514).

On page 511, Opalinska et al. teach the unpredictability of nucleic acid molecules to modulate the expression of their intended targets *in vivo* as following:

“Nucleic-acid-mediated gene silencing has been used with great success in the laboratory, and this strategy has also generated some encouraging results in the clinic. Nevertheless, it is widely appreciated that the ability of nucleic-acid molecules to modify gene expression *in vivo* is quite variable, and therefore wanting in terms of reliability. Several issues have been implicated as a root cause of this problem, including molecule delivery to targeted cells and specific compartments within cells, and identification of sequence that is accessible to hybridization in the genomic DNA or RNA....Accordingly, mRNA targeting is largely a random

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process, which accounts for the many experiments in which the addition of an antisense nucleic acid yields no effect on expression.”

Further, the unpredictability of *in vivo* inhibitory activity, let alone therapeutic efficacy, of siRNA molecules remains unresolved even after the filing date of this application as taught by Schmidt (*Nature Biotechnology*, 2007, 25:273-275). As Schmidt discusses several RNAi patents, he points out that “Though RNAi has become invaluable for basic research, its therapeutic potential is unknown. Delivering RNAi drugs to target cells poses difficult challenges; largely because of this, drug-development with RNAi remains mainly in preclinical stages.” (page 273)

In light of the teachings of both Opalinska et al. and Schmidt, one of ordinary skill in the art would not have practiced the entire scope of the claimed invention solely based on the *in vivo* examples comprising a single antisense oligonucleotide species: SEQ ID NO:12. Again, SEQ ID NO:12 is not the nucleotide sequence applicant elected. Since there is neither positive *in vitro* – *in vivo* correlation for the elected SEQ ID NO:10 nor sufficient *in vivo* data for treating or preventing cancer comprising any oligonucleotide inhibitor other than the exemplified antisense oligonucleotide comprising SEQ ID NO:12, and since the general teachings in the art are such that nucleic-acid based therapeutics still remain highly unpredictable, one of ordinary skill in the art would not have practiced the instantly claimed *in vivo* therapeutic methods with a resultant “treatment” or “preventative” effect in a mammal by administering any oligonucleotide inhibitor targeted to MBD2 gene at the time the invention was made.

*In re Vaeck*, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991), the Court ruled that a rejection under 35 U.S.C. 112, first paragraph for lack of enablement was appropriate given the relatively incomplete understanding in the biotechnological field involved, and the lack



of a reasonable correlation between the narrow disclosure in the specification and the broad scope of protection sought in the claims.

In view of all the factors listed above and the totality of the teachings that the activity of nucleic-acid based drugs including siRNAs is unpredictable *in vivo*, undue experimentation would have been required of a skilled artisan to practice the entire scope of the instantly claimed invention. Since the issues described above are not satisfactorily resolved herein, it is concluded, based on the evidence as a whole, that the instant specification fails to teach how to use the claimed invention without undue experimentation, and that the scope of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims.

***Claim Rejections - 35 USC § 112, second paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 11 provides for the use of the oligonucleotide inhibitor of claim 1 or the vector or claim 8, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

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Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 11 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-2 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Zannis et al. (US 5,877,009).

The claims are drawn to an oligonucleotide inhibitor, wherein the inhibitor is an antisense oligonucleotide comprising at least 7 consecutive nucleotides of SEQ ID NO:10, wherein the inhibitor inhibits expression of a mammalian MBD2/demethylase gene.

Zannis et al. teach a 30-mer oligonucleotide comprising SEQ ID NO:66, 15 consecutive nucleotides of which are in perfect sequence alignment with instantly claimed SEQ ID NO:10. See below for the sequence alignment between SEQ ID NO:10 of the instant case ("Qy") and SEQ ID NO:66 of Zannis et al. ("Db").

Qy	3	CTCTCCCCCTCCCCC	17
Db	3	CTCTCCCCCTCCCCC	17

Since the oligonucleotide comprising SEQ ID NO:66 of Zannis et al. meets the structural requirement set forth in the claims, the isolated oligonucleotide sequence of Zannis et al. will inherently inhibit expression of a mammalian MBD2/demethylase gene, absent evidence to the contrary.

Claims 1-2 and 5 are rejected under 35 U.S.C. 102(e) as being anticipated by Wohlgemuth et al. (US 6,905,827 B2).

The claims are described above.

Wohlgemuth et al. teach a 50-mer oligonucleotide comprising SEQ ID NO:8110, 14 consecutive nucleotides of which perfectly align with the claimed antisense oligonucleotide sequence SEQ ID NO:10. See below for sequence alignment.

Qy	5	CTCCCCCTCCCCCT	18
Db	6	CTCCCCCTCCCCCT	19

Since the oligonucleotide comprising SEQ ID NO:8110 of Wohlgemuth et al. meets the structural requirement set forth in the claims, the isolated oligonucleotide sequence of Wohlgemuth et al. will inherently inhibit expression of a mammalian MBD2/demethylase gene, absent evidence to the contrary.

Claims 1-2, 8-11, 22, 24-25, 27-29, and 31 are rejected under 35 U.S.C. 102(e) as being anticipated by Bigey et al. (US 2006/0009403 A1).

The claims are drawn to an antisense oligonucleotide, vector, a host cell, and a pharmaceutical composition comprising the antisense oligonucleotide complementary to a mammalian MBD2/demethylase mRNA, wherein the oligonucleotide inhibits expression of the MBD2/demethylase mRNA, wherein the oligonucleotide is about 7 to about 100 nucleotides in length, and the methods of treating cancer in a mammal comprising administering the antisense oligonucleotide, wherein the oligonucleotide inhibits cancer growth and the cancer is lung cancer, and the mammal is a human.

Bigey et al. teach an antisense oligonucleotide targeted to MBD2/demethylase gene, wherein the oligonucleotide comprises at least 15 consecutive nucleotides (paragraphs 0012-0019). They teach a vector comprising the antisense oligonucleotide, further comprising a pharmaceutically acceptable carrier (paragraphs 0032-0033). They teach a host cell into which the vector containing the antisense oligonucleotide is transferred (paragraph 0036). They teach a method of treating cancer by introducing a vector expressing the antisense oligonucleotide targeted to MBD2/demethylase gene, wherein the growth of human tumors is inhibited *in vivo* (paragraphs 0038-0040). In particular, they show reduction of tumor size in mice implanted with human non-small cell lung tumor cells. See Example 1.

Accordingly, all the limitations set forth in claims 1-2, 8-11, 22, 24-25, 27-29, and 31 are taught by Bigey et al.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-11 and 22-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Slack et al. (*The Journal of Gene Medicine*, Published online May 17, 2002, 4:381-389, citation of record) in view of McKay et al. (US 5,877,309), Walton et al. (*The Biomedical Engineering Handbook*, 2000, Second Edition, Chapter 103), and Elbashir et al. (*Genes & Development*, 2001, 15:188-200).

The claims are drawn to an oligonucleotide inhibitor, wherein the inhibitor is an antisense oligonucleotide, a ribozyme, and an siRNA comprising at least 7 consecutive nucleotides of SEQ ID NO:10, wherein the inhibitor inhibits expression of a mammalian MBD2/demethylase gene,

wherein the oligonucleotide inhibitor comprises phosphorothioates and 2'-O-methyl modifications, and a method of treating lung cancer in a human.

The specification, especially Figure 3, teaches that instant SEQ ID NO:10 (represented as A6) is located within the 5'-UTR of the MBD2 gene.

Slack et al. teach that a vector comprising antisense MBD2/demethylase cDNA inhibits tumor growth in mice transplanted with non-small lung cancer cells (pages 385-388). They teach that MBD2 is a candidate target gene for antisense gene therapy in cancer (page 388). Slack et al. do not teach an antisense oligonucleotide, a ribozyme, and an siRNA comprising at least 7 consecutive nucleotides of SEQ ID NO:10, nor do they teach phosphorothioate and 2'-O-methyl modifications.

McKay et al. teach that most preferred target region of a gene for antisense oligonucleotides includes the 5'-UTR. See column 5, lines 12-14.

Walton et al. teach that antisense technology utilizing RNase H-mediated target mRNA degradation, such as antisense oligonucleotides and ribozymes, is useful for cancer treatment. They teach that chemical modifications such as phosphorothioates and 2'-O-methyl help increase binding affinity for the target mRNA and also reduce nuclease-mediated degradation. See entire reference. They teach that antisense compounds comprising 2'-O-methyl and/or phosphorothioate modifications have been tested for clinical trials for treatment of cancer. See Table 103.2.

Elbashir et al. teach that siRNAs cleave target RNA via RNA interference (page 188). They teach that siRNAs may represent a new alternative to antisense or ribozyme therapeutics (page 198).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to replace the antisense cDNA vector of Slack et al. with the antisense oligonucleotide, ribozyme, or siRNA of Walton et al. or Elbashir et al., by targeting the 5'-UTR of the MBD2 gene sequence as taught by McKay et al.

One of ordinary skill in the art would have been motivated to modify the teachings of Slack et al. in view of the combined teachings of Walton et al. and Elbashir et al., with a reasonable expectation of success, because the instant target gene, MBD2, was known to be involved in tumorigenesis, and therefore inhibiting the gene expression via antisense construct was shown to be effective in reducing tumor size in mice, as taught by Slack et al. (page 388), and because phosphorothioate and 2'-O-methyl-modified antisense oligonucleotides and ribozymes were known to be effective in cancer treatment by increasing stability and specificity as taught by Walton et al., and because siRNA molecules were known to be a new alternate gene therapy agent in place of antisense oligonucleotides or ribozymes as of the earliest filing date sought in the instant application, as taught by Elbashir et al. (page 198). The skilled artisan would have been further motivated to target the 5'-UTR of the MBD2 gene of Slack et al., because McKay et al. expressly teach that the 5'-UTR is one of the most preferred target regions for antisense oligonucleotides (column 5, lines 12-14). Since the instantly claimed antisense oligonucleotide sequence SEQ ID NO:10 is found to be located in the 5'-UTR as evidenced by Figure 3 of the instant application, the skilled artisan would have had a reasonable expectation of success in making an antisense oligonucleotide comprising at least 7 consecutive nucleotides of SEQ ID NO:10 through routine screening and optimization experimentation, in view of the

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specific teachings of McKay et al. (column 5, lines 12-14). Accordingly, the instantly claimed invention taken as a whole would have been *prima facie* obvious at the time of filing.

### ***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dana Shin whose telephone number is 571-272-8008. The examiner can normally be reached on Monday through Friday, from 8am-4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin  
Examiner  
Art Unit 1635

*/J. E. Angell/*  
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